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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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In re Application of:

JUKARAINEN et al.

Serial No.: 09/701,547

Group Art Unit: 1712

Filed: November 30, 2000

Examiner:

For: A MEMBRANE OR MATRIX FOR CONTROLLING THE PERMEATION RATE OF DRUGS

**INFORMATION DISCLOSURE STATEMENT
PURSUANT TO 37 CFR 1.97(b)**

Commissioner for Patents
Washington, D.C. 20231

February 28, 2001

Sir:

The attention of the Patent and Trademark Office is hereby directed to the documents listed on the attached Form PTO-1449. One copy of each document is attached.

The listed documents marked with an asterisk were cited in a search report for the corresponding Finnish and/or International Applications. Copies of the Finnish and PCT search reports are attached.

European Patent Publication No. 545 002 discloses silicone polymers grafted with polyoxyalkylene groups. These polymers are paste-like and they are intended to increase viscosity in silicone oils. Europe '002 does not mention elastomers prepared from these polymers. The polymers can also not be crosslinked. Further, Europe '002 does not propose anything that would lead to the

conclusion that the polymers may be used in membranes or matrices for controlling the release rate of a drug. Europe '002 is therefore not relevant to the present invention.

Europe Patent Publication No. 882 753 was published after the priority date of this application, and discloses silicone-based gels and pastas directed to increase the viscosity of fluids. Gels are formed by adding a large quantity of solvent (page 5, line 34: 80-98 wt-% of the composition). Although Europe '753 uses the word "elastomer", the applicant is of the opinion that it is used incorrectly. According to the examples, the amount of non-crosslinked material is high (90%). An elastomer is in the art known as a continuous network, non-deformable and stable. Especially in the application of controlling the permeation of drug, stability is an essential feature of the product and gels could not be used in such applications. To be successfully used in controlled drug delivery formulations, a material must be chemically inert and free of leachable impurities. On page 6, lines 2-3 of Europe '753, it is mentioned that the products according to the invention may be used as carriers for pharmaceutical drugs. A carrier is, however, a completely different product from a membrane or matrix controlling the release rate of the drug. A carrier may be any non-toxic product that can be mixed with the drug. A carrier does not need to affect the

release rate of the drug and it may decompose as soon as the device has been introduced to its final place. In contrast, a membrane or a matrix controlling the release rate of a drug has to remain stable as long as there is any drug left in the device. Europe '753 is therefore not relevant to the present invention.

Finnish application 973 427 was published after the priority date of this application. The Finnish application is the priority application of C-I-P Application S.N. 09/442,403, in the name of the applicant.

Ullman et al. discloses films prepared from block copolymers comprising PEO and PDMS and the permeation of different steroids through these films. One has, however, to bear in mind that according to claim 1 of the present invention, one condition is that the poly(alkylene oxide) groups that are present as alkoxy-terminated grafts or blocks of the polysiloxane units are linked to the polysiloxane units by silicon-carbon bonds. In Ullman et al., the PEO groups are not linked to the PDMS groups by silicon-carbon bonds, but by urea bonds. The block copolymers of Ullman et al. also give totally different results than the elastomer compositions according to the invention: in Ullman et al. it is stated that the increase of PEO in block copolymer increases the permeation of hydrophilic steroids, whereas the permeation of lipophilic steroids decreases. In this invention, the increase of PEG groups always

increases the permeation rate of the drug regardless of the lipophilic or hydrophilic nature of the drug (Specification, page 29, lines 22-26). In addition to that, the block copolymer described Ullman et al. has a very complicated structure and synthesis, and could therefore not be used widely in industry. Ullman et al. is thus not relevant to the present invention.

An English translation of Chemical Abstracts 126:2000090 is attached. On page 1 of the translation, it is said that a siloxane-based polymer bearing pendant long-chain alkyl ether groups is useful in blended silicone rubber. However, Chemical Abstracts '090 is concerned only with simple ether groups, whereas the invention requires poly(alkylene oxide) groups, that is, successive ether groups. The invention is also surprising in view of Chemical Abstracts '090: according to this invention, increasing the amount of polyalkylene groups increases the permeation rate of the drug (Specification, page 29, lines 22-26). A polymer bearing ether groups according to Chemical Abstracts '090 has a completely opposite effect to the permeation rate of the drug: table 4 on page 6 shows that addition of polymer bearing ether groups slows the permeation rate of the drug, because the highest rate was achieved with PDMS, which does not contain ether groups. The slowing effect might be caused by the fact that the alkyl group of the ether is very long, that is, it contains at least ten carbon atoms, whereas

U.S. Patent Appln. S.N. 09/701,547
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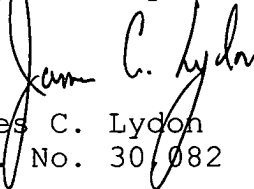
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in this invention, the corresponding group is very small. Chemical Abstracts '090 is therefore not relevant to the present invention.

U. S. Patent No. 5,884,108 corresponds to EP 882 753.

No fee or certification is required in connection with this Information Disclosure Statement, since it is being submitted prior to the last of (1) issuance of a first official action on the merits and (2) expiration of the three month period following filing of the above-captioned application. Nevertheless, the Commissioner is authorized to charge our Deposit Account No. 50-1258 for any fee which is deemed by the Patent and Trademark Office to be required to effect consideration of this statement. Two copies of this authorization are attached.

Respectfully submitted,



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Attachments:
Form PTO-1449;
9 References;
PCT Search Report; and
Finnish Search Report